REMARKS

By the amendments presented, Claim 40 has been canceled without prejudice.

Also by the amendments presented, Claim 36 has been amended to more specifically recite that the claimed mucoretentive composition is an aqueous mucoretentive composition. Support for this amendment is found in originally filed Claim 1.

Also by the amendments presented, Claims 36 and 38 have been amended to recite that the claimed mucoretentive composition comprises colloidal particles of "silicon dioxide" rather than stating colloidal particles of "silica".

Also by the amendments presented, Claim 37 has been amended to more specifically recite the by weight concentrations of the claimed citric acid component. Support for this amendment is found in the specification at page 3, line 1, and page 16, lines 33-36.

Also by the amendments presented, Claim 39 has been amended to more specifically recite the mean particle size of "silicon dioxide" rather than reciting the mean particle size of "colloidal silica". Support for this amendment is found in the specification at page 9, lines 3-4.

Also by the amendments presented, Claim 41 has been amended to depend from Claim 38 rather than from canceled Claim 40, and to more specifically recite the selected group of "silicon dioxide" rather than "colloidal silicon dioxide" components. Support for this amendment is found in the specification at page 8, lines 32-35.

Also by the amendments presented, new Claim 42 has been added to more specifically recite a salt of the claimed citric acid component. Support for the amendment is found in the specification at page 17, lines 1-2.

Also by the amendments presented new Claims 43-48 have been added to recite claim language limited to an oral, mucoretentive, aqueous liquid, and pharmaceutical composition. Support for these amendments is found in originally filed Claims 1 and 11, and in the specification at page 3, line 1, page 8, lines 26-34, page 9, lines 3-4, page 16, lines 33-36, and page 17, lines 1-2.

Attached hereto is a marked-up version of the changes made to the claims as a result of the current amendments. The attached page is captioned **"Version with Markings to Show Claim Changes Made"**.

Upon entry of the amendments presented, Claims 36-39, and 41 remain in this continuation examination application. Claims 42-48 are new in the application. No additional claims fee is due.

Invention Synopsis

The present invention is directed to oral, liquid, aqueous, mucoretentive compositions, and a method of administering such compositions, wherein the compositions comprise colloidal particles of silicon dioxide and a select pharmaceutical active.

It has been found that prolonged and improved coating and protection of components of the alimentary canal such as the stomach, esophagus, and small int stine can b achieved by incorporating a mucoadhesive material into an oral pharmaceutical composition. Unlike

conv ntional mucoadhesiv materials such as mucoadhesive polymers, the compositions of the present invention omprise a silicon dioxide which provid s for highly effective mucoadh siv systems.

Formal Matters

In the Amendment dated July 8, 2002, which was acknowledged as being received by the PTO on July 9, 2002, Applicant requested cancellation of Claims 31 and 33-35. Applicant then stated that Claims 30-35 have been canceled. For clarification, Applicant hereby submits that Claims 30-35 are to be canceled in the present application as a result of the Amendment dated July 8, 2002.

Art Rejections

a) **Rejection under 35 U.S.C. 102**

Claims 36, 38, and 40-41 have been rejected under 35 U.S.C. 102 as being anticipated by Chavkin et al. (U.S. Patent 4,980,175). The Examiner contends that Chavkin et al. disclose an oral, liquid composition as claimed by Applicant, wherein the composition comprises colloidal silicon dioxide and a pharmaceutical active selected from gastrointestinal agents. Applicant submits that Claim 40 has been canceled without prejudice, thus obviating this rejection as it would apply to this claim. Applicant respectfully traverses this rejection as it would apply to amended Claims 36, 38, and 41.

Chavkin et al. disclose orally ingestible liquid compositions that are non-aqueous liquid suspension systems comprising from about 1% to about 90% by weight of colloidal silicon dioxide, a pharmaceutical active such as gastrointestinal agents, at least one triglyceride or propylene glycol ester of a medium chain length alkanoic acid, and a polyglycerol ester. Chavkin et al. further disclose that the non-aqueous, orally ingestible liquid compositions can also comprise known bio-adhesive agents such as polycarbophil and the alginates. Chavkin et al., however, fail to disclose an aqueous mucoretentive composition and a method of administering such an aqueous composition.

Applicants submit that the Chavkin et al. reference fails to anticipate Applicant's Claims 36, 38 and 41, as amended, because this particularly applied reference fails to teach an aqueous mucoretentive composition and a method of administering the composition. Chavkin et al. teach non-aqueous orally ingestible liquid compositions, not Applicant's now claimed aqueous mucoretentive composition that is administered by oral ingestion.

In view of the foregoing remarks, it is submitted that the Chavkin et al. reference fails to teach Applicant's now claimed limitations of Claims 36, 38, and 41, wherein these claims are now limited to a method of administering an active agent selected from gastrointestinal agents by swallowing an aqueous mucoretentive composition comprising from about 2% to about 50% by weight of colloidal particles of silicon dioxide. Therefore, the Chavkin et al. reference fails to anticipate Applicant's Claims 36, 38, and 41. Accordingly, the rejection of these claims as being anticipated by Chavkin et al. is improper, and should be withdrawn.

b) Rejection under 35 U.S.C. 103

Claims 36-41 been rejected under 35 U.S.C. 103 as being unpatentably obvious over Chavkin et al. (U.S. Patent 4,980,175). The Examiner contends that Chavkin et al. disclose a mucoretentive composition as claimed by Applicant and that it would have been obvious based on the teachings of Chavkin et al. to administer such a mucoretentive composition to the stomach, notwithstanding Chavkin et al.'s failure to specifically disclose a citric acid component as claimed by Applicant. Applicant submits that Claim 40 has been canceled without prejudice, thus obviating this rejection as it would apply to this claim. Applicant respectfully traverses this rejection as it would apply to amended Claims 36-39, and 41.

Chavkin et al. disclose orally ingestible liquid compositions that are non-aqueous liquid suspension systems comprising from about 1% to about 90% by weight of colloidal silicon dioxide, a pharmaceutical active such as gastrointestinal agents, at least one triglyceride or propylene glycol ester of a medium chain length alkanoic acid, and a polyglycerol ester. Chavkin et al. further disclose that the non-aqueous, orally ingestible liquid compositions can also comprise known bio-adhesive agents such as polycarbophil and the alginates, and optionally contain ingredients known for special purposes such as flavors, colors, natural and artificial sweeteners, preservatives, and silicone antiflatulent actives. Chavkin et al., however, fail to disclose an aqueous mucoretentive composition and a method of administering such an aqueous composition.

Applicant submits that the Chavkin et al. reference would not obviously lead the skilled artisan to a realization of Applicant's invention of Claims 36-39 and 41, as amended. Chavkin et al. fail to teach or suggest an aqueous mucoretentive composition and a method of administering the composition. The Chavkin et al. reference teaches and suggests orally ingestible liquid compositions that are non-aqueous suspension systems. By contrast, Applicant's amended Claim 36-39 and 41 are now limited to a method of administering an orally ingestible aqueous mucoretentive composition.

The Examiner contends that it would have been prima facie obvious to realize Applicant's invention of remaining Claims 36-39 and 41 based on the teachings of the Chavkin et al. reference. Applicant disagrees as this particularly applied reference relates to amended remaining Claims 36-39 and 41. Applicant submits that the Chavkin et al. reference teaches and suggests non-aqueous compositions, and Chavkin et al. states at col. 1, lines 30-44 that aqueous systems are disadvantageous and that non-aqueous liquid suspension systems are desirable. Therefore, the Chavkin et al. reference only provides motivation for administering non-aqueous orally ingestible liquid compositions, not Applicant's now claimed aqueous mucoretentive composition, prima facie or otherwise.

In view of the foregoing remarks, it is submitted that the Chavkin et al. reference fails to teach or suggest a method of administering an active agent by swallowing an aqueous mucoretentive composition as now recited in Applicant's Claims 36-39 and 41. R jection of these claims, as

amended, as being unpatentably obvious over Chavkin et al. is improper and, therefore, should be withdrawn.

Conclusions

Applicant has made an earnest effort to place his application in proper form and to distinguish his claimed invention from the applied prior art. WHEREFORE, reconsideration of this application, withdrawal of the rejections under 35 U.S.C. 102 and 103, and allowance of Claims 36-39, and 41-48 are respectfully requested.

Respectfully submitted,
Douglas J. Dobrozsi

By Joan B. Cunningham
Joan B. Cunningham
Agent for Applicant
Registration No. 43,962
(513) 622-3993

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Cincinnati, Ohio
Customer No. 27752

Version with Markings to Show Claim Changes Mad

Claims 36-39, and 41 have been amended as follows:

Claim 36. (Amended) A method of administering an active agent to one or more of th esophagus, stomach, and small intestine by swallowing a safe and effective amount of a mucoretentive composition comprising from about 2% to about 50%, by weight of the composition, of colloidal particles of [silica] silicon dioxide and a safe and effective amount of a pharmaceutical active selected from the group consisting of gastrointestinal agents, analgesics, decongestants, expectorants, antitussives, antihistamines, bronchodilators, topical anesthetics, sensory agents, and mixtures thereof, wherein the mucoretentive composition is an aqueous mucoretentive composition.

Claim 37. (Amended) The method of Claim 36 wherein the mucoretentive composition further comprises from about 0.005% to about 3% by weight of citric acid or a salt thereof.

Claim 38. (Amended) The method of Claim 36 wherein the mucoretentive composition is not further diluted with any liquid prior to administration and the level of colloidal particles of [silica] silicon dioxide is from about 3% to about 15%, by weight of the mucoretentive composition.

Claim 39. (Amended) The method of Claim 36 wherein the [colloidal silica] silicon dioxide has a mean particle size of less than about 1 micron.

Claim 41. (Amended) The method of Claim [40] 38 wherein the [colloidal] silicon dioxide is selected from the group consisting of fumed silicon dioxide, precipitated silicon dioxide, coacervated silicon dioxide, gel silicon dioxide, and mixtures thereof.

The following new Claims 42-48 have been added:

--Claim 42. The method of Claim 36 wherein the salt of citric acid is sodium citrate.--

--Claim 43. An oral, mucoretentive, aqueous liquid, pharmaceutical composition comprising:

(c) from about 2% to about 50%, by weight of the composition, of colloidal particles of silicon dioxide; and

(d) a safe and effective amount of a pharmaceutical active selected from the group consisting of gastrointestinal agents, analgesics, decongestants, expectorants, antitussives, antihistamines, bronchodilators, topical anesthetics, sensory agents, and mixtures thereof.--

--Claim 44. The oral, mucoretentive, aqueous liquid, pharmaceutical composition of Claim 43 wh rein the composition comprises from about 3% to about 20% by weight of the colloidal particles of silicon dioxide.--

--Claim 45. Th oral, mucoretentive, aqueous liquid, pharmaceutical composition of Claim 44 wherein the silicon dioxid has a mean particle size of less than about 1 micron.--

--Claim 46. The oral, mucoretentive, aqueous liquid, pharmaceutical composition of Claim 43 wherein the silicon dioxide is selected from the group consisting of fumed silicon dioxide, precipitated silicon dioxide, coacervated silicon dioxide, gel silicon dioxide, and mixtures thereof.--

--Claim 47. The oral, mucoretentive, aqueous liquid, pharmaceutical composition of Claim 43 wherein the composition further comprises from about 0.005% to about 3.0% by weight of citric acid or a salt thereof.--

--Claim 48. The oral, mucoretentive, aqueous liquid, pharmaceutical composition of Claim 47 wherein the salt of citric acid is sodium citrate.--